Correlation of transthoracic echocardiography-derived pulmonary to systemic flow ratio with hemodynamically estimated left to right shunt in atrial septal defects

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ABSTRACT

Background : **Transthoracic echocardiographic (TTE) estimation of the pulmonary to systemic flow ratio (Qp/Qs) is routinely used in clinical practice and is included in the American Society of Echocardiography Guidelines. We sought to assess its real-world applicability with a particular focus on hemodynamically significant shunt lesions.**

Methods : **Retrospective single institutional review of TTE's in patients with secundum atrial septal defect prior to cardiac catheterization (cath) from 2012 to 2018 was performed (n = 109), those with technically limited images for Qp/Qs calculation (n = 11) and those with time interval between TTE and cath >60 days were excluded (n = 14). Qp/Qs was calculated from stored clips by previously described methods and correlated with those obtained by oximetry. Patients were subdivided into two age groups <21 (Group 1) and ≥22 years (Group 2). TTE and cath methods for Qp/Qs estimation were compared using paired t-test, Pearson's correlation coefficient, and Bland–Altman plots.**

Results : **Eighty-four subjects met inclusion criteria (age range 3–78 years). Group 1 n = 35; median age 10 years; Group 2 n = 49; median age 49 years. Transthoracic echocardiogram was performed 19.5 ± 15 days prior to cath. Mean Qp/Qs derived by cath and TTE were 2.09 ± 0.9 versus 2.54 ± 1.2 (P < 0.0001). Overall correlation was poor between the methods (r^2 = 0.32, P < 0.0001) and continued to be poor for Groups 1 and 2 (r^2 = 0.24, P = 0.003 and r^2 = 0.40, P < 0.0001 respectively). Bland–Altman plots demonstrated poor agreement between the predetermined limits of agreement (−0.5–1.5).**

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Conclusion : **Transthoracic echocardiography estimated Qp/Qs, although routinely utilized in clinical practice, has poor correlation and agreement with oximetry-derived Qp/Qs. The test performs poorly in all age groups in detecting a hemodynamically significant shunt and tends to overestimate the degree of left to right shunt.**

Keywords : Atrial septal defect, left to right shunt, oximetry, transthoracic echocardiography

INTRODUCTION

Transthoracic echocardiographic (TTE) Doppler estimation of blood flow has been in routine clinical use since its description. It is derived as the product of the cross-sectional area (CSA) and the average velocity of the blood cells passing through the blood vessel or valve orifice during the flow period.[1,2] As such, stroke volume (SV) represents the product of velocity-time integral (VTI) and the CSA of the respective site. This principle can theoretically be used in patients with shunt due to septal defects to calculate the pulmonary to systemic flow ratio (Qp/Qs); a left to right shunt results in higher pulmonary blood flow compared to systemic or aortic flow resulting in higher Qp/Qs. TTE estimation of the Qp/Qs has been validated with oximetry in a small number of children and young adults.[3-7] It is routinely used in clinical practice by cardiologists who do not routinely deal with congenital cardiac lesions as a noninvasive tool to estimate left to right shunt. Furthermore, the American Society of Echocardiography 2015 guidelines for the echocardiographic assessment of atrial septal defect (ASD) reports the possibility of estimating shunt flow by pulsed Doppler quantification of the Qp/Qs ratio.[8] However, in practice and in the best of hands, these calculations are subject to ~20% measurement error.[1] We sought to assess real-world correlation of TTE estimation of Qp/Qs and its applicability with particular focus on hemodynamically significant ASD shunt lesions.

METHODS

Patient selection

A retrospective single institutional review of TTE's in patients with secundum ASD prior to cardiac catheterization was performed. All patients with a secundum ASD who underwent a cardiac catheterization for device closure between January 2012 and January 2018 who underwent cardiac cath and TTE within 60 days were included. Patients with additional congenital heart disease such as ventricular septal defects, patent ductus arteriosus or associated lesions as stenosis or regurgitation of the aortic and pulmonary valves and patients with suboptimal images in which the diameters of their pulmonary orifices could not be visualized or with suboptimal hemodynamic data to estimate Qp/Qs were excluded. The study population consisted of 109 patients with a secundum type ASD. The patients ranged in age from 3 to 78 years. Patients were subdivided into two age groups, age <21 years (Group 1) and ≥22 years (Group 2) to assess the influence of age. Eleven of the 109 patients with ASD were excluded because the diameters of their pulmonary orifices could not be visualized by echocardiography or there were no Doppler recordings of the pulmonary annulus to be able to obtain hemodynamic data. An additional 14 patients were excluded because the time interval between cardiac cath and TTE was >60 days. In the other 84 patients, all Doppler and echocardiographic images obtained were satisfactory. All patients underwent diagnostic cardiac catheterization with attempted or successful device closure of an ASD. Two subjects younger than 3 years underwent sedated echocardiograms as per our laboratory protocol.

Ultrasound measurements

TTE stored clips and Doppler recordings of the left and right ventricular (RV) outflow tracts were retrospectively reviewed for each patient, these measures included electrocardiogram so that they can be appropriately timed. Using previously described methods to estimate pulmonic and aortic outflow, recorded left ventricular (LV) outflow velocity and RV outflow velocity clips were identified, and VTI was

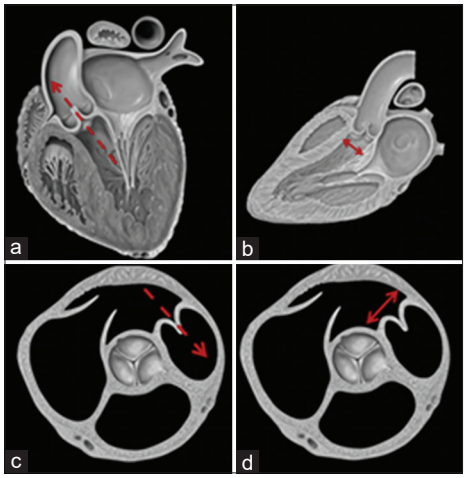

Figure 1: Illustrations demonstrating the measurement of flow velocity (red dotted arrow) (a) and diameter (b) of the left ventricular outflow tract (red solid double headed arrow), and the measurement of the flow velocity (red dotted arrow) (c) and diameter (d) of the right ventricular outflow tract (red solid double headed arrow).

measured, each observation was measured twice and averaged for the analysis. Figure 1 depicts illustrations demonstrating measurements of flow velocity and diameters of the outflow tracts. The time velocity curve of a pulsed Doppler sample at the outflow was digitized to obtain the VTI.[1] As recommended when tracing the velocity to derive a VTI, tracings were obtained at the outer edge of the most dense (or brightest) portion of the spectral tracing.[1] Pulsed Doppler velocities were used, as this ensures that the velocity sample is obtained at the vascular inlet where the flow profile is most flat.[9,10] If continuous wave Doppler is used, there is error in the peak velocity due to the sampling of more distal flow in which there is more flow acceleration. The diameters of aortic and pulmonic orifices were measured at the level of the respective annulus. The CSA of each orifice was then calculated:

$$CSA = \pi (diameter/2)^2$$

The SV was then calculated as the product of CSA and Doppler VTI. Assuming the velocity profile at the semilunar valve orifice is flat, the right and LV (Left ventricular) SV s were determined as products of CSA and the velocity integral over systole:

$$SV = CSA \times VTI$$

Cardiac catheterization measurements

All patients underwent cardiac catheterization for hemodynamic assessment and secundum ASD device closure or attempted device closure under general anesthesia. The hemodynamic data were reviewed retrospectively, and the Qp/Qs ratio calculated by Fick method (using the blood oxygen content in the pulmonary artery, pulmonary vein, systemic artery, and mixed venous blood) was recorded.[11] All the catheterization parameters were obtained twice and averaged, the cath measures and calculations were obtained by a single observer (BL).

Data analysis

Results of the Doppler and cardiac catheterization Fick methods for measuring systemic and pulmonary blood flow and Qp/Qs ratio were compared using paired *t*-test, Pearson's correlation coefficient, and Bland–Altman plots. We used limits of agreement of – 0.5 and 1.5 for Bland–Altman plots to be clinically acceptable. A probability value (*P*) <0.05 was considered statistically significant.

Reproducibility

The TTE measures were performed in all subjects retrospectively by a single observer (EF), inter-observer and intra-observer agreement was tested for absolute agreement of Echo derived Qp/Qs in a randomly selected sample ($n = 20$) by two observers (EF and SCU). Reproducibility was analyzed by intra-class correlation coefficients (ICC); the point estimates and the 95% confidence intervals (CI) of the agreement rate were reported. Statistical analyses were performed using MedCalc for Windows, version 20.009 (MedCalc Software, Ostend, Belgium).[12]

RESULTS

Eighty-four subjects met inclusion criteria (age range 3–78 years). Group 1 had 35 subjects with median age of 10 years (range 3–21 years); Group 2 had 49 subjects with a median age of 47 years (range 22–78 years). TTE was performed 19.5 ± 15 days prior to cath. The longest interval between Doppler examination and cardiac catheterization was 58 days. Overall, the mean Qp/Qs derived by TTE was significantly higher than cath (2.54 ± 1.2 vs. 2.09 ± 0.9; $P < 0.0001$). Furthermore, the overall correlation was poor between the two methods [$r^2 = 0.32$, $P < 0.0001$; Figure 2].

For Group 1, mean Qp/Qs derived by cath and TTE was 1.94 ± 0.8 and 2.53 ± 1.1 respectively ($P = 0.002$). The mean Qp/Qs derived by cath for Group 2 was 2.19 ± 0.8 compared to TTE 2.55 ± 1.2 ($P < 0.01$). Consistent with the overall poor correlation, the correlation continued to be poor for both Groups 1 and 2 [$r^2 = 0.24$, $P = 0.003$ and $r^2 = 0.40$, $P < 0.0001$ respectively; Figure 3a and b].

The Doppler and cardiac catheterization Fick methods estimations of Qp/Qs were compared using Bland–Altman plots to determine how well the methods were in agreement. We used limits of agreement of – 0.5 and 1.5 for Bland–Altman plots to be clinically acceptable. Figure 4 shows a Bland–Altman plot of the difference between Echo and cath estimated Qp/Qs plotted against the mean of echocardiogram and cath derived Qp/Qs. The overall mean difference between Echo and cath derived Qp/Qs is 0.44 with 95% CI – 1.5–2.4. The

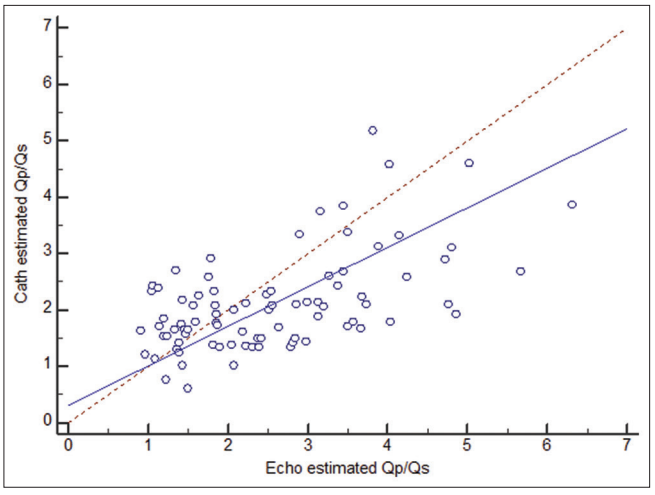

Figure 2: Estimated Qp/Qs by echo and Qp/Qs estimated by cath, with line of equality. Qp/Qs: Pulmonary to systemic flow ratio

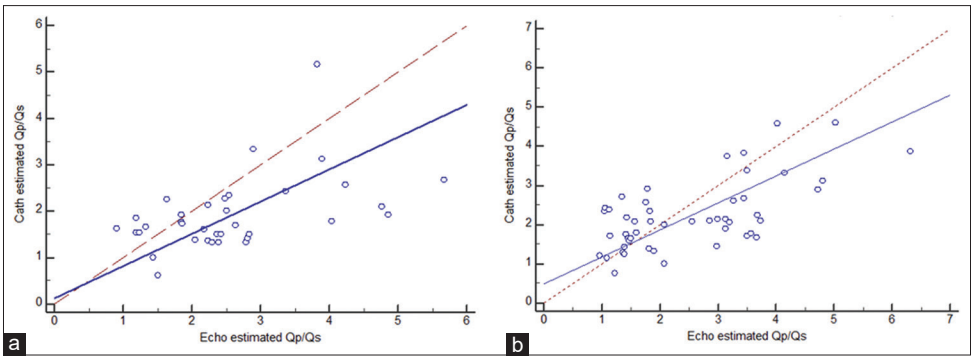

Figure 3: Estimated Qp/Qs by echo and Qp/Qs estimated by cath for subjects <21 yo (a) and for subjects ≥22 yo (b). Qp/Qs: Pulmonary to systemic flow ratio

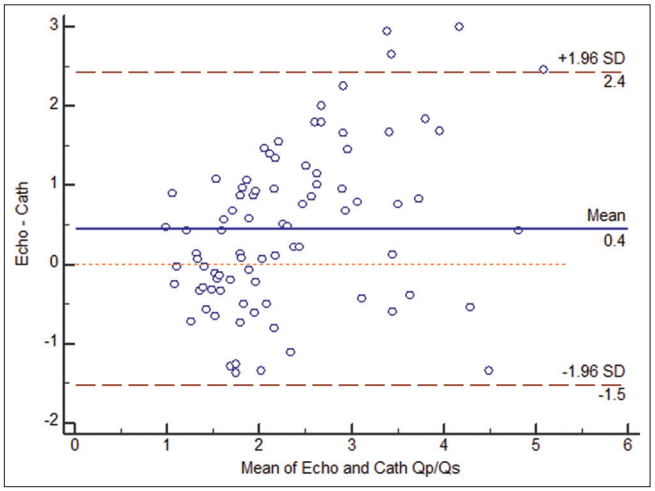

Figure 4: Difference of echo and cath estimated Qp/Qs against mean Qp/Qs. Qp/Qs: Pulmonary to systemic flow ratio

agreement is poor between the two methods within the predetermined limits of agreement (–0.5 and 1.5) and, therefore not acceptable. As shown in Figure 4, many points fall outside the limits of agreement of clinical acceptance, and therefore the two methods are not interchangeable. The agreement for the difference in shunt size was also investigated with Bland–Altman plots. For patients with a Qp/Qs ratio < 1.5, the difference between echo and cath Qp/Qs was again plotted against the mean [Figure 5a]. Using the same limits of agreement of – 0.5 and 1.5, the agreement is stronger for patients with a hemodynamically insignificant shunt size. However, the agreement worsened with increasing shunt size. Bland–Altman plots for cath derived Qp/Qs for shunt >1.5, and >2.0 are shown in Figure 5b and c, respectively. Therefore, the agreement for patients with hemodynamically significant shunts was poor and did not fall within the limits of agreement.

Inter-observer agreement between two observers (EF and SCU) for twenty random subjects was good for Echo derived Qp/Qs (ICC: 0.89; 95% CI 0.61 – 0.96). Intra-observer agreement for one observer (EF) was also good (ICC: 0.97; 95% CI 0.92–0.98).

DISCUSSION

In this study, we found TTE estimated Qp/Qs, although routinely utilized in clinical practice, has poor correlation with oximetry derived Qp/Qs and tended to overestimate left to right shunt.

TTE estimation of the Qp/Qs was previously validated with oximetry in a small number of children and young adults.[3,4,6] Dittmann *et al.* prospectively obtained echocardiographic images of 16 patients with ASDs and found the two methods correlated well, but that with increasing shunt size, error increased.[6] Other small sample studies found similar results.[3,5,7] Although measurements of blood flow in the aorta and pulmonary artery using Doppler techniques appear straightforward in principle, there are several practical problems limiting its use and accuracy.

It is well described that to best accurately estimate blood flow, it is important to match the site of velocity measurement with the site of CSA measurement. In order to prevent measurement error, it is also important to use the region where the flow profile is laminar and flat and is preferable to use sites where the CSA does not change significantly during the flow period.[1] The preferred region to best estimate SV is the LV outflow tract or aortic annulus followed by mitral and pulmonary annulus. The pulmonic annulus is difficult to visualize due to poor lateral resolution and thus limits its accuracy, especially in those with poor acoustic windows. The RV outflow tract is dynamic and contracts during systole.[1]

We theorize the biggest source of error is the measurement of Qp/Qs is due to anatomic measurement issues. Measurement of the pulmonary valve orifice is subject to greater error than the aortic valve, due to poorer visualization of the pulmonary valve.[10,13] When measuring the pulmonary valve orifice, measurements are made from short-axis views that tend to have low lateral resolution.[9] These technical factors lead to inaccurate measurements of the pulmonary annulus diameter. Additionally, the RV outflow tract is dynamic

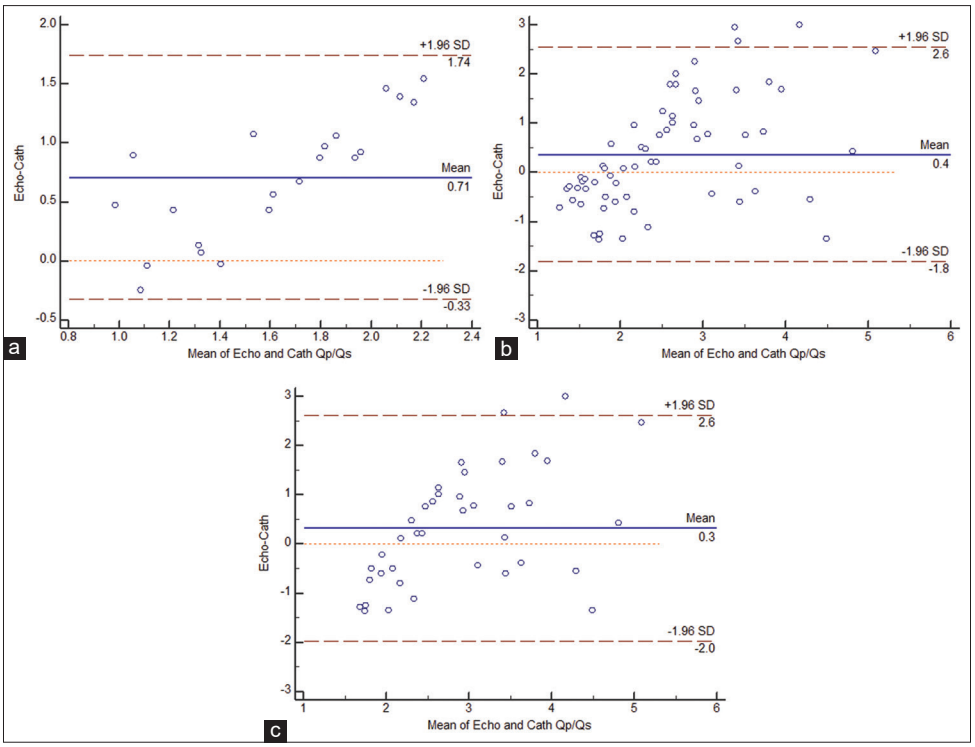

Figure 5: Difference between echo and cath estimated Qp/Qs against mean Qp/Qs for cath Qp/Qs <1.5 (a) difference between echo and cath estimated Qp/Qs against mean Qp/Qs for cath Qp/Qs >1.5 (b) difference between echo and cath estimated Qp/Qs against mean Qp/Qs for cath Qp/Qs >2.0 (c). Qp/Qs: Pulmonary to systemic flow ratio

and contracts during systole thus resulting in significant diameter changes with cardiac cycle. Studies have shown that the CSA of the aorta increases 5%–10% during systole, while that of the pulmonary artery increases up to 18%.[3] This finding can be exaggerated in ASD when there is increased Qp/Qs resulting in further increase in the RV SV. As Colan points out in his review of hemodynamic assessment, even small measurement errors of the valve orifice can be significant, as the annulus diameter is then squared in the calculation of CSA.[9,10] Therefore, a 10% error in measurement in the diameter results in a 19% error in CSA. Furthermore, this error is further amplified because Qp/Qs is a ratio. In the example Colan provides, if a pulmonary valve diameter of 10 mm is mismeasured as 9 mm, the resulting error in Qp/Qs is 25%,[10] a small error in measurement has a large impact on the measurement of Qp/Qs.[9] Because of the amplification of errors in measuring the annulus using CSA, a simplified equation to approximate Qp/Qs using just the ratio of peak velocities and ratio of the annulus diameter of the pulmonary and aortic valves has been suggested: $Qp/Qs = [PkV_{PA}/PkV_{AO}] \times [D_{PA}/D_{AO}]^2$,[[13-15]] but its clinical applicability needs further testing.

There is also a potential error when measuring flow velocity using Doppler measurements. The flow velocity measured by Doppler technique is essentially the cosine function of the angle between the Doppler beam and flow vector. Therefore, the Doppler incident angle needs to be taken into careful account. When the incident angle exceeds a critical value (more than 20 degrees), it can cause an error in accurately determining flow velocity.[4] In a study by Kitabatake *et al.*, echocardiographic Doppler images were obtained of 22 patients with an ASD. When obtaining Doppler recordings of flow velocity, they were careful in maintaining the Doppler beam directed as parallel as possible to the long axis of the RV outflow tract and LV outflow tract flow. However, they report that even with careful consideration of the incident angle, they failed to set the Doppler incident angle at < 20° in the RVOT in 9 of 22 patients and in the LV outflow tracts of 18 of 22 patients. In adult patients with ASD, the right ventricle often presents with more marked dilatation than it does in children because of the long persistence of the RV volume overload. In such cases, the alignment of the Doppler beam parallel to the flow vector is likely more difficult.[4] With long-standing significant left to right shunt, the flow pattern across the pulmonary valve is altered secondary to increase flow, and flow profile may not remain flat.

A recent large retrospective study involving 2797 subjects, tested RVOT VTI as the single echocardiographic parameter and were able to identify hemodynamically significant shunting in those with high RVOT VTI (≥25 cm) where the traditional calculations as reported above have been either impossible or not practical for various reasons in the real world setting.[16]

A hemodynamically significant left to right shunt is an indication for surgical or transcatheter closure of an ASD. Therefore, a reported echocardiogram estimated Qp/Qs shunt size of >1.5 or 2 has a significant clinical impact. The Bland–Altman plots demonstrated that for patients with a deemed hemodynamically less significant shunt, or <1.5, had fair agreement within the deemed limits of agreement. However, for patients with hemodynamically significant shunts and thus an indication for intervention, the agreement was poor, and therefore, echocardiographic estimation of Qp/Qs is not interchangeable with a cardiac Fick estimation of Qp/Qs. It is most important in these patients with hemodynamically significant shunts for there to be a strong agreement.

Study limitations

This study was a single-center retrospective analysis. Additionally, the time between echocardiogram and cardiac catheterization was on average 19.5 days. Although for most patients the time interval was 30 days or less, there were several patients with a >1 month interval between echocardiogram and cardiac cath. It is possible the clinical condition of patients changed for the patients with a greater interval between echocardiogram and catheterization although we strongly believe shunt in ASD is related to relative compliance of the pulmonary and systemic circulations, and thus time intervals between the modalities of few weeks are unlikely to result in significant hemodynamic changes.

CONCLUSIONS

Transthoracic echocardiography estimated Qp/Qs although routinely utilized in clinical practice has poor correlation and agreement with oximetry-derived Qp/Qs. The test performs poorly in all age groups, it is not interchangeable with a cardiac Fick estimation of Qp/Qs and tends to overestimate the degree of the left to right shunt.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA; Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: A report from the Doppler quantification task force of the nomenclature and standards committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002;15:167-84.
2. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1- 39.e14.
3. Sanders SP, Yeager S, Williams RG. Measurement of systemic and pulmonary blood flow and QP/QS ratio using Doppler and two-dimensional echocardiography. Am J Cardiol 1983;51:952-6.
4. Kitabatake A, Inoue M, Asao M, Ito H, Masuyama T, Tanouchi J, *et al.* Noninvasive evaluation of the ratio of pulmonary to systemic flow in atrial septal defect by duplex Doppler echocardiography. Circulation 1984;69:73-9.
5. Vargas Barron J, Sahn DJ, Valdes-Cruz LM, Lima CO, Goldberg SJ, Grenadier E, *et al.* Clinical utility of two-dimensional doppler echocardiographic techniques for estimating pulmonary to systemic blood flow ratios in children with left to right shunting atrial septal defect, ventricular septal defect or patent ductus arteriosus. J Am Coll Cardiol 1984;3:169-78.
6. Dittmann H, Jacksch R, Voelker W, Karsch KR, Seipel L. Accuracy of Doppler echocardiography in quantification of left to right shunts in adult patients with atrial septal defect. J Am Coll Cardiol 1988;11:338-42.
7. Zoghbi WA, Quinones MA. Determination of cardiac output by Doppler echocardiography: A critical appraisal. Herz 1986;11:258-68.
8. Silvestry FE, Cohen MS, Armsby LB, Burkule NJ, Fleishman CE, Hijazi ZM, *et al.* Guidelines for the echocardiographic assessment of atrial septal defect and patent foramen ovale: From the American Society of Echocardiography and Society for cardiac angiography and interventions. J Am Soc Echocardiogr 2015;28:910-58.
9. Colan SD. Hemodynamic Measurements. In: Lai WW, Mertens LL, Cohen MS, Geva T, editors. Echocardiography in pediatric and congenital heart disease. Oxford, UK: Wiley-Blackwell; 2009. p. 63–75. doi:10.1002/9781444306309.ch6.
10. Colan SD. Quantitative applications of Doppler cardiography in congenital heart disease. Cardiovasc Intervent Radiol 1987;10:332-47.
11. Bergersen L, Foerster S, Marshall, AC, Meadows J. ASD device closure. In: Congenital Heart Disease. Bergersen L, Foerster S, Marshall AC, Meadows J, editors. US: Springer; 2009. p. 115-8. [doi: 10.1007/978-0-387-77292-9_17].
12. MedCalc Software Ltd. MedCalc® Statistical Software. Ostend, Belgium: MedCalc Software Ltd; 2021.
13. Friedberg MK. Hemodynamic Measurements. In: Lai WW, Mertens LL, Cohen MS, Geva T, editors. Echocardiography in pediatric and congenital heart disease: from fetus to adult. Oxford, UK: John Wiley & Sons, Ltd; 2016. p. 73-95. doi:10.1002/9781118742440.ch6

14. Silverman NH. Pediatric Echocardiography. Baltimore: Williams & Wilkins; 1993. p. 628.
15. Oh JK, Seward JB, Tajik AJ. The Echo Manual. 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2007. p. 431.
16. Dannenberg V, Goliasch G, Hengstenberg C, Binder T, Gabriel H, Schneider M. Detection of atrial shunt lesions with a single echocardiographic parameter. Wien Klin Wochenschr 2020;132:295-300.